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and so far, this seems very safe. We agree that the PERTs are multidisciplinary and are similar to our group. In fact, Dr Barnes is the head of the PERT group at Michigan. A major question not answered yet is whether invasive therapies for diagnosed pulmonary artery embolism or thrombosis would be of benefit in the COVID-19-infected patients.

Thus, in agreement with Porres-Aguilar and colleagues, some form of multidisciplinary team to help manage the COVID-19-related thrombotic diagnoses and treatment makes much sense and will help add to the experience in treating these extremely challenging patients.

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<https://doi.org/10.1016/j.jvsv.2020.05.014>

Use of low-molecular-weight heparin in COVID-19 patients



Marone and Rinaldi¹ in their study reported cases of deep venous thrombosis (DVT) in hospitalized patients with 2019 novel coronavirus disease (COVID-19). We appreciate the efforts by the authors to present preliminary data on COVID-19-related DVT in their practicing institution and to discuss the possible underlying mechanisms of DVT.

According to the authors, administration of anticoagulant/therapeutic doses of low-molecular-weight heparin (LMWH) in hospitalized COVID-19 patients, instead of prophylactic doses, is the current practice in their practicing institution. Although some may have concern of increased risk of bleeding, bleeding does not appear to be a major manifestation of COVID-19. A higher than traditional standard prophylactic dose of LMWH as adopted in the authors' institution should be encouraged because there is possibly more risk of venous thromboembolism in hospitalized COVID-19 patients than in their non-COVID-19 counterparts.

Particularly, Middeldorp et al² reported that about 20% of the included COVID-19 patients had venous

thromboembolism despite routine thromboprophylaxis with prophylactic doses of LMWH. A comparison with the largest randomized controlled trial thus far of LMWH for the prevention of venous thromboembolism in acutely ill medical patients (non-COVID-19) that reported a thromboprophylaxis failure rate of only 2.77% indicated that the standard prophylactic dose of LMWH in COVID-19 patients may be inadequate.

A higher than usual rate of thromboprophylaxis failure may be due to an increasingly recognized hypercoagulable state with COVID-19 in which a number of changes in circulating prothrombotic factors have been reported in COVID-19 patients: elevated factor VIII level, elevated fibrinogen level, circulating prothrombotic microparticles, and presence of neutrophil extracellular traps.^{3,4} These prothrombotic changes are not usually detected in acutely ill medical patients without COVID-19, in whom the efficacy of standard prophylactic dosing of LMWH is established.

In addition, it has become increasingly clear that obesity is one of the biggest risk factors for severe COVID-19 disease, and therefore obese patients may constitute a significant proportion of hospitalized COVID-19 patients.⁵ Because high body weight correlates with low anti-factor Xa levels, an anti-factor Xa-guided individualized dosing approach with LMWH may also be adopted in the obese hospitalized COVID-19 population to further reduce the risk of thromboprophylaxis failure. We look forward to studies reporting outcomes on anti-factor Xa-guided approach for dosing of LMWH among COVID-19 patients.

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<https://doi.org/10.1016/j.jvsv.2020.06.006>

Reply



The remarks made by Kow and Hasan¹ regarding the use of low-molecular-weight heparin (LMWH) in hospitalized COVID-19 patients are greatly appreciated since they focus on one of the most important aspects concerning the treatment of this disease, namely, thromboprophylaxis. In fact, since our latest letter was published in this *Journal*, suggesting a close correlation between COVID-19 and deep venous thrombosis (DVT),² a number of studies have followed, confirming this view and providing evidence of the fact that respiratory infection is also responsible for a systemic procoagulant activity,³⁻⁵ which can lead to different clinical manifestations ranging from DVT to septic intravascular coagulation, not only in the most critical cases (patients in intensive care unit) but in all in-hospital patients. In light of this evidence, heparin has become a cornerstone of the treatment against COVID-19, along with empirical antiviral and antibiotic therapy, but the correct dose to administer is still the subject of discussion.⁶ Most centers continue to administer a prophylactic dose of LMWH (100 mUI/kg daily), although our experience reports several cases of DVT and pulmonary embolism in COVID-19 patients with this posology, which justifies the use of anticoagulant doses (100 mUI/kg twice a day) when no absolute contraindication to anticoagulant therapy exists. This is, in our opinion, a correct approach, although there are other potential risks to be taken into account, for example, thrombocytopenia, a common alteration in COVID-19 patients that is a predictor of poor prognosis and can be worsened by LMWH.⁷ The decision is, in fact, a difficult one, and it is made even harder by the many things that we still ignore regarding the effects that the virus has on the hemostatic function. In this respect, constant and careful monitoring of platelet count and coagulation parameters (especially D-dimer and fibrinogen) throughout the entire clinical course is crucial to recognize and minimize complications.

In conclusion, we share the authors' view that COVID-19 is a powerful risk factor for DVT; moreover, in hospitalized patients, it is often associated with pre-existing comorbidities (advanced age, obesity) and immobilization that further enhance the thrombotic risk, and so all measures should be adopted to counteract the onset of DVT or other clinical manifestations of an altered hemostasis. To this purpose, further studies investigating the relationship between disease severity and the extent

of coagulopathy will be necessary to select those patients who need more protection.

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Inconsistency of salvage outcome data in extremity vein repair versus ligation using the National Trauma Data Bank



The recently published "Impact of ligation vs repair of isolated popliteal vein injuries on in-hospital outcomes in trauma patients" by Byerly et al¹ gave us the opportunity to review multiple publications of traumatic vein injury repair based on the National Trauma Data Bank (NTDB). This retrospective study